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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/727,696	12/03/2003	Chaitan Khosla	300622000508	8649

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EXAMINER	
NASHED, NASHAAT T	
ART UNIT	PAPER NUMBER
1656	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/727,696	KHOSLA ET AL.	
	Examiner	Art Unit	
	Nashaat T. Nashed, Ph. D.	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 7-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 7-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/4/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The application has been amended as requested in the communication filed November 10, 2006. Accordingly, claims 1 and 7 have been amended, and claims 6 and 14-30 have been canceled.

Claims 1-5, and 7-13 are under consideration in this Office action.

The terminal disclaimer filed on November 10, 2006 disclaiming the terminal portion of any patent granted on this application, which would extend beyond the expiration date of U. S. patent 6,391,594 has been reviewed and is accepted. The terminal disclaimer has been recorded.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 and 7-14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons set forth in the prior Office action mailed 5/10/06.

Applicants have failed to provide any argument for the rejection under 35 USC 112, first paragraph, for lack of written description.

Claims 1-5 and 7-14 are rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement of the full scope of the claimed invention for the reasons set forth in the prior Office action mailed 5/10/06.

In response to the above rejection, applicants argue that the have taught a generic method applicable to any AT domain from any gene cluster, even those to be discovered yet.

Applicants' arguments filed 11/10/06 have been fully considered but they are not deemed to be persuasive. Enablement requires a disclosure sufficient to allow a person of skill in the art to practice the full scope of the claimed invention without undue experimentation. The previous Office action sets out a *prima facie* case of non-enablement, explaining by sound scientific reasoning why a person of ordinary skill in the art would doubt that the guidance of the specification would enable practice of the full scope of the claimed invention without undue experimentation. Applicants have presented no evidence or, indeed, any arguments to establish the adequacy of the

disclosure to enable the scope of the instant claims. Applicants merely assert that they have disclosed a general method applicable to any modular PKS once it becomes available. The scope of enablement is related to the state of the prior art. If applicant is claiming a generic method using known materials, applicants may be entitled to generic method. In another word, if at the time of invention there was a sufficient known species to support the genus claimed method, the generic claims are fully enabled even if there were species to be discovered yet. In contrast, if the number of species at the time of invention available in the prior art does not support a genus claim, the generic method clearly lacks enablement. Applicants make no effort to explain why they consider the disclosure of two examples would be sufficient enablement for the full scope of the claimed genus. Conclusory statements unsupported by evidence or scientific reasoning are insufficient to overcome the *prima facie* case of non-enablement set out in the previous Office action.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-5 and 7-14 are rejected under 35 U.S.C. § 102(b) as being anticipated by Katz *et al.* (Katz, WO 93/13663) for the reasons set forth in the prior Office action mailed 5/10/06.

Claims 1-5 and 7-14 are rejected under 35 U.S.C. § 102(e) as being anticipated by U. S. P 5,824,513 ('513, IDS reference number 5) for the reasons set forth in the prior Office action mailed 5/10/06.

In response to the above rejection, applicants appear to agree that the cited references above appear to be the same. They argue that there is no place in the application wherein the substitution of an AT domain by another is described. Although applicants appear to agree that the AT domain is taught in the cited documents as the one which select the appropriate enantiomer, they argue that the cited art does not state that extender unit is specified by the AT function of erythromycin. In addition, applicant argue that claim 1 in the '513 patent is quite different as the claim directed to a different method in which a domain is isolated mutated and reinserted.

Applicants' arguments filed 11/10/06 have been fully considered, but they are found unpersuasive. Enantiomers are optical isomers and are not considered the same molecule. Enantiselectivity is an integral part of substrate specificity and can't be separated for applicants' from one another. It is agreed that the prior art teach that the AT domain responsible for selecting the appropriate enantiomer, i.e., the appropriate substrate to incorporate into the polyketide. Thus, it is a *prima facie* teaching that the AT domain determine the structure of the extender unit. The '513 patent and its claims is an issued patent, and its compliance with the various statute and rules as well as its validity is presumed. Applicants allege that claim 1 is different from the claimed method. The examiner disagrees. First, the claimed method is fully described in the description and specification of the cited art. The entire application is directed to various methods of engineering diversity in a gene cluster to produce novel polyketide. The voluminous description in both documents described in details the various modifications that can be mad in the gene cluster including the substitution of an acytransferase domain. Applicant attention is directed to claim 1 in the '513 patent (corresponds to claim 16 of the '663 document), wherein the alteration in step (c) is specified as substitution of the AT domain by another in part (vi). Claim 1 of the '513 patent states [see in particular, the underline part in (c)]:

> A method for directing the biosynthesis of a specific erythromycin analog by genetic manipulation of a gene encoding the deoxyerythronolide B synthase function of an erythromycin-producing microorganism, said method comprising the steps of:
>
> (a) isolating a genomic DNA segment comprising the eryA gene of Saccharopolyspora erythraea;
>
> (b) identifying discrete fragments of said genomic DNA each encoding a separate polypeptide domain, wherein each domain provides no more than one of the enzymatic activities associated with said deoxyerythronolide B synthase function, said enzymatic activities consisting of .beta.-ketoreductase, dehydratase, acyl carrier protein, enoylreductase, .beta.-ketoacyl ACP synthase and acyltransferase;
>
> (c) altering at least one region of said eryA gene by modifying said DNA fragments to produce at least one alteration of said deoxyerythronolide B synthase function, said alteration selected from the group consisting of (i) inactivation of one or more domains providing enzymatic activity affecting the processing of .beta.-carbonyl groups of polyketide subunits, (ii) addition of one or more domains providing enzymatic activity affecting the processing of .beta.-carbonyl groups of polyketide subunits, (iii) inactivation of one or more domains providing enzymatic activity affecting the condensation of carbon units to a nascent deoxyerythronolide B structure, (iv) addition of domains providing enzymatic activities affecting the length of said deoxyerythronolide B structure, (v) deletion of one or more domains providing one or more enzymatic activities affecting the length of said deoxyerythronolide B structure, and (vi) substitution of one

acyltransferase domain with another isologous acyltransferase domain of different specificity;

(d) transforming a cell of said erythromycin-producing microorganism with said altered region of said eryA gene under conditions suitable for the occurrence of a homologous recombination event replacing a corresponding region of said cell's eryA gene with said altered region;

(e) growing a culture of said transformed cell under conditions suitable for the formation of said specific erythromycin analog; and

(f) isolating said specific erythromycin analog from said culture.

Thus, the prior art describe and taught the claimed invention and therefor, the claims remain rejected.

Claims 1-14 are rejected under 35 U.S.C. § 102(e) as being anticipated by U. S. P 6,200,813 ('813, IDS reference number 14) for the reasons set forth in the prior Office action mailed 5/10/06.

Applicants argue that he '813 patent is matured from a continuation in part application from that matured the '513 patent, and therefore not all information in the patent is a qualified prior art against the instant application.

Applicants' arguments filed 11/10/06 have been fully considered, but they are found unpersuasive. Claim 1 of the '513 patent is fully enabled and described in the application which the '513 patent matured from. Applicants are correct in that the application matured to '613 patent is a continuation in part from that matured to the '513 patent. Applicant should note that the method of claim 1 of the '513 and '813 patent would be expected to produce the same result. Since claim 1 of the '513 patent is enabled in its application, the '813 patent claims are enabled in the parent application. The only difference between the two claim is that the claim of the '513 patent is broader in scope than that of the '813 patent. The two claims have overlapping scoop, which contains the claimed subject matter of the instant application. Thus, the claims remain rejected.

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is 571-272-0934. The examiner can normally be reached on MTWTF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen K. Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nashaat T. Nashed, Ph. D.
Primary Examiner
Art Unit 1656